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Data Evaluation Report on the Reproductive Effects of Metaldehyde Technical on Mallard Duck, Anas platyrhynchos

PMRA Submission Number

EPA MRID Number 42867902

Data Requirement:

PMRA DATA CODE EPA DP Barcode

OECD Data Point

EPA MRID EPA Guideline 42867902 OPP §71-4b

Purity: 99%

Date:

Signature:
Date: 1/4/05

Signature:
Date: 1/20/05

Date: Collect M Haber 07 Feb 05

Test material:

Metaldehyde Technical

Common name:

Metaldehyde

Chemical name:

IUPAC: Not reported CAS name: Not reported

CAS No.: 9002-91-2 Synonyms: None reported

Primary Reviewer: Christie E. Padova Staff Scientist, Dynamac Corporation

QC Reviewer: Teri Myers

Staff Scientist, Dynamac Corporation

Primary Reviewer: Colleen Flaherty OPP/EFED/ERB - III

Secondary Reviewer(s):

{EPA/OECD/PMRA}

Reference/Submission No.:

Company Code: Active Code:

EPA PC Code:

053001

Date Evaluation Completed:

CITATION: Beavers, J.B., and K.A. Hoxter, and M. Jaber. 1993. A Reproduction Study with Metaldehyde in the Mallard. Unpublished study performed by Wildlife International Ltd., Easton, MD. Laboratory Project No. 289-107. Study submitted by Lonza Inc., Fair Lawn, NJ. Study initiated April 1, 1992, and submitted August 3, 1993.

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EPA MRID Number 42867902

EXECUTIVE SUMMARY:

The one-generation reproductive toxicity of Metaldehyde Technical to groups (16 pens/treatment level) of 1 male and 1 female, 19-week-old Mallard duck was assessed over approximately 22 weeks. Metaldehyde Technical was administered to the birds in the diet at nominal concentrations of 0 (negative control), 50, 175, and 500 ppm. Mean-measured concentrations were <LOD (control), 49, 176, and 497 ppm a.i., respectively.

There were no significant treatment-related effects on adult mortality, body weight, or feed consumption at any test level. However, three hens from the 497 ppm a.i. level exhibited convulsive behavior during washing procedures. Episodes occurred in single birds during Weeks 12, 19, and 20. In all cases, the hens appeared to recover completely within 15 minutes of the episode and the clinical signs did not re-occur. The LOAEC for clinical signs of toxicity in adult birds was 497 ppm a.i. Although not conclusive as related to treatment, the incidence of the numbers of regressing/regressed ovaries observed upon necropsy of hens totaled 7/15, 11/16, 10/15, and 14/16 for the control, 49, 176, and 497 ppm levels, respectively.

The reviewer's analysis detected significant reductions in the ratios of number hatched to eggs laid, to eggs set, and to live embryos at all treatment levels, as well as in the ratio of hatchling survival to eggs set at the lowest treatment level. As a result, the NOAEC for these reproductive endpoints could not be determined (<49 ppm). At the measured 497 ppm level, treatment-related effects were observed on eggs set, number hatched, hatchling survival, and the ratio of hatchling survival to number hatched.

No overt signs of toxicity were observed in hatchlings from the control, 49, or 176 ppm levels, and no treatment-related effect on offspring body weights were observed at any treatment level. Offspring from the 497 ppm level displayed profound clinical signs that appeared to be treatment related. In general, up to approximately one-third of the offspring hatched in any given week displayed dorsal or ventral neck curl, and circling behavior. Furthermore, the ducklings from this level appeared more excitable and disoriented than normal offspring. In a number of cases, the ducklings that survived appeared to improve as they matured. The LOAEC for effects on reproduction was 497 ppm.

This study is scientifically sound, but it does not fulfill the guideline requirements for a reproductive toxicity study with mallard duck (§71-4b) because a NOAEC could not be identified. As a result, this study is classified as Supplemental.

Results Synopsis

Test Organism Size/Age: 19 weeks old at test initiation (955 -1430 g)

NOAEC: <49 ppm a.i. LOAEC: 49 ppm a.i.

Endpoint(s) Affected: Clinical signs of toxicity (adults and offspring), eggs set, number hatched, ratio of number hatched to eggs laid, number hatched to eggs set, number hatched to live embryos, hatchling survival, ratio of hatchling survival to eggs set, and hatchling survival to number hatched.

PMRA Submission Number

EPA MRID Number 42867902

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED:

The study protocol was based on procedures of the U.S. EPA Pesticide Assessment Guidelines, §71-4 (1982). Deviations from §71-4 are:

1. Mortality of the Mallard during acclimation was not reported.

2. Since effects on reproduction were observed, a withdrawal period should have been conducted.

3. The LOD/LOQ for the analytical method was not reported.

4. The expected field residue level was not reported.

5. The average egg storage temperature (prior to setting for incubation) was 14.2°C, slightly lower than the recommended level of 16°C.

 A NOAEC was not identified in this study because significant effects on reproduction were detected at the lowest treatment level.

Failure to detect a NOAEC affected the acceptability of the study; the study is classified as supplemental.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. This study was conducted in accordance with United States, OECD, and Japan MAFF GLP standards, with the following exceptions: the physical and chemical characterization of the test substance was not performed at the laboratory, and was considered the responsibility of the sponsor; periodic analysis of basal diet and water for background concentrations of selected organic and inorganic substances were not fully conducted in compliance with GLP standards; there were two instances during the conduct of the study where a daily balance check was not property documented. Historical data for this balance indicated that these two occurrences had no scientific impact on the study.

A. MATERIALS:

1. Test Material

Metaldehyde Technical

Description:

Off-white powder

Lot No./Batch No.:

5448

Purity:

.99%

Stability of Compound

Under Test Conditions:

The stability of Metaldehyde Technical in the treated feed was assessed during the pilot study in treated feed prepared at 300, 1000, and 2000 ppm and stored in open metal bird feeders under ambient conditions for 10 days. Initial (Day 0) recoveries ranged from 100.6 to 105.5% of nominal concentrations, and final (Day 10) recoveries ranged from 97.8 to 105.2%

of nominal concentrations.

Storage conditions of test chemical:

The test substance was transferred from the shipping containers into perforated cardboard containers lined with plastic, to allow for air circulation throughout the containers. The containers were covered, and stored refrigerated at approximately 5°C. These procedures were performed in order to allow for the release of any acetaldehyde that may be formed during the degradation of metaldehyde, as acetaldehyde is

considered a catalyst for further degradation.

Stability of Compound

(Neat) Under

Storage conditions:

The storage stability of Metaldehyde Technical (neat) was assessed periodically from receipt (10/91) to the end of the definitive study (9/92) using gas chromatography. Recoveries were ≥99.60% metaldehyde and

≤0.40% acetaldehyde for all samples.

OECD requires water solubility, stability in water and light, pK_{ω} , P_{ow} and vapor pressure of the test compound. The following OECD requirements were reported:

Aqueous solubility:

Approx. 300 ppm (temperature not specified)

2. Test organism:

Table 1: Test organism.

Parameter	Details	Remarks Criteria
Species (common and scientific names):	Mallard duck (Anas platyrhynchos)	EPA: a wild waterfowl species, preferably Anas platyrhynchos, or an upland game species, preferably Colinus virginianus.
Age at Study Initiation:	19 weeks	Birds were reportedly approaching their first breeding season.
		EPA requires: birds should be approaching their first breeding season.
Body Weight: (mean and range)	Males: Overall range (n=64) 1024 to 1430 g, with group means of 1216 to 1235 g.	Individual body weights were recorded at Weeks 0, 2, 4, 6, 8 and 22 (test termination).
	Females: Overall range (n=64) 955 to 1280 g, with group means of 1064 to 1087 g.	EPA: body weights should be recorded at test initiation and at biweekly intervals up to week 8 or up to the onset of egg laying and at termination.
Source:	Whistling Wings, Inc. Hanover, IL	Birds were from the same hatch, and were phenotypically indistinguishable from wild birds.
		EPA: that all birds should be from the same source.

B. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study - A 6-week pilot study was conducted with an unspecified number of adult Mallard at nominal dietary concentrations of 300, 1000, and 2000 ppm. Three birds from the 1000 ppm group and all birds from the 2000 ppm group died prior to study termination. In addition, there were decreases in body weight and feed consumption at 2000 ppm, and decreases in egg production at the 1000 and 2000 ppm levels.

EPA MRID Number 42867902

b. Definitive Study

Parameter	Details	Remarks
		Criteria
Acclimation period: Conditions (same as test or not): Feeding:	3 weeks Same as test Water and feed were provided ad libitum.	At test initiation, all birds were examined for physical injuries and general health, and birds that did not appear healthy were excluded from the study. Ducks were fed a basal game-bird diet formulated by Agway Inc., to meet laboratory specifications, and provided public tap water from Easton, MD.
Health (any mortality observed):	Pre-test mortality was not reported.	EPA: 2-3 week health observation period prior to selection; birds must be generally healthy without excess mortality; feeding should be <u>ad libitum;</u> sickness, injuries or mortality be noted.
Test duration pre-laying exposure:	Approximately 10 weeks	Reproductive effects were observed; a withdrawal period should have been conducted.
egg-laying exposure: withdrawal period, if used:	Approximately 12 weeks None	EPA requires Pre-laying exposure duration: > 10 weeks prior to the onset of egg-laying. Exposure duration with egg-laying: > 10 weeks. Withdrawal period: If reduced reproduction is evident; < 3 weeks added to the test phase.
Pens size: construction materials:	Parents (one pair) were housed in battery breeding cages measuring 75 x 90 x 45 cm. Offspring (by set and group) were housed in 62 x 92 x 25.5 cm battery brooders. Parental pens were constructed of vinyl-coated wire mesh. Offspring pens were constructed of vinyl-coated wire mesh and stainless steel sheeting.	Pens Adequate room and arranged to prevent cross contamination Materials Nontoxic material and nonbinding material, such as galvanized steel. Number At least 5 replicate pens are required for mallards housed in groups of 7. For other arrangements, at least 12 pens are required, but considerably more may be needed if birds are kept in pairs. Chicks are to be housed according to parental grouping.
Number of birds per pen (male:female)	2 birds/pen (1 male:1 female)	EPA: 1 male and 1 female per pen. For ducks, 2 males and 5 females is acceptable.

EPA MRID Number 42867902

Parameter	Details	Remarks
		Criteria
# Pens/treatment negative control: solvent control: treated:	16 pens N/A 16 pens/treatment	EPA requires at least 12 pens, but considerably more if birds are kept in pairs. At least 16 is strongly recommended.
Test concentrations (ppm diet) nominal: measured:	0 (negative control), 50, 175, and 500 ppm <lod (control),="" (reviewer-calculated)<="" 176,="" 49,="" 497="" a.i.="" and="" ppm="" td=""><td>Samples used for concentration verification analyses were collected from freshly-prepared diets prior to study Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 21; recoveries from 91.4 to 112.6% nominal; LOD/LOQ not reported; concentrations of test substance in diet not adjusted for purity</td></lod>	Samples used for concentration verification analyses were collected from freshly-prepared diets prior to study Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 21; recoveries from 91.4 to 112.6% nominal; LOD/LOQ not reported; concentrations of test substance in diet not adjusted for purity
		EPA: ≥ 2 concentrations other than the control are required; three or more are recommended
Maximum labeled field residue anticipated and source of information:	Not specified	EPA: highest test concentrations should show a significant effect or be at or above the actual or expected field residue level.
Solvent/vehicle	None used	EPA requires corn oil or other appropriate vehicle not more than 2% of diet by weight
Was detailed description and nutrient analysis of the	Yes	Basal diets contained ≥27% protein, ≥2.5% fat, ≤5% fiber, and 5% limestone. Offspring received basal diet test substance or limestone.
basal diet provided? (Yes/No)		EPA requires a commercial breeder feed (or its equivalent) that is appropriate for the test species.

Parameter	Details	Remarks
		Criteria
Preparation of test diet	Test substance was combined directly with a small portion of basal ration, mixed using Waring blender, quantitatively transferred with basal ration as the rinsing agent to a Hobart mixer containing additional basal feed. Remaining ration was added and mixed for 20 minutes. Separate pre-mixes were prepared for each concentration level every 4 weeks; stored frozen until needed. Final diets were prepared weekly. Portions of pre-mix were combined with additional basal ration and limestone, mixed for 20 minutes in a Patterson-Kelly Twin Shell blender prior to offering.	No solvents or carriers were used in diet preparation. A premixed containing the test substance should be mechanically mixed with basal diet. If an evaporative vehicle is used, it must be completely evaporated prior to feeding.
Stable and homogeneous?	Yes	
Were concentrations in diet verified by chemical analysis?	Yes	Samples were analyzed from feed prepared during Weeks 1, 2, 3, 4, 8, 12, 16, 20, and 21. Recoveries for all toxicant levels ranged from 91.4-112.6% of nominal concentrations.
Did chemical analysis confirm that diet was stable?	Yes	Stability was assessed during the pilot study in treated feed prepared at 300, 1000, and 2000 ppm and stored in open metal bird feeders under ambient conditions for 10 days. Initial (Day 0) recoveries 100.6-105.5% nominal; final (Day 10) recoveries 97.8-105.2% of nominal concentrations. Details of the were not provided.
Homogeneous?	Yes	Homogeneity was assessed in prepared on Day 0 of Week 1 at 50 and 500 ppm treatments. Six samples per level were collected: 1/side from the top, middle, and bottom of batch. Calculated CVs were 5.8% at at the 500 ppm
Feeding and husbandry	Feeding/husbandry conditions appeared to be adequate	

Parameter	Details	Remarks			
		Criteria			
Test conditions (pre- laying) $20.9 \pm 1.7^{\circ}$ C temperature: $71 \pm 17\%$		Light intensity averaged 365 lux. Illumination was provided by fluorescent lights which closely approximated noon-day sunlight.			
relative humidity: photo-period:	8 hr light/day up through Week 8; 17 hr light/day thereafter.	EPA Requires Temperature: About 21°C (70°F) Relative humidity: About 55% Lighting <u>First 8 weeks</u> : 7 h per day; <u>Thereafter</u> : 16-17 h per day. At least 6 foot candles at bird level.			
Egg Collection and Incu	ıbation				
Egg collection and storage collection interval: storage temperature:	Daily 14.2 ± 1.0 °C	Collected eggs were washed in a commercial egg washer with chlorine-based detergent at 46°C for 3 minutes; washed eggs were allowed to cool to room temperature and rinsed with fresh water prior to storage.			
storage humidity:	$84 \pm 15\%$	EPA: eggs collected daily; storage temperature 16°C (61°F); humidity 65%.			
Were eggs candled for cracks prior to setting for incubation?	Yes	EPA requires eggs to be candled on day 0			
Were eggs set weekly?	Yes				
Incubation conditions temperature: humidity:	37.5 ± 0.0°C Approx. 56%				
When candling was done for fertility?	Day 14 for embryo viability and Day 21 for embryo survival.	EPA: Quail approx. day 11; duck approx. day 14			
When eggs were transferred to hatcher	Day 24	EPA: Bobwhite day 21; mallard day 23			
Hatching conditions temperature: humidity: photo-period:	37.2 ± 0.0°C Approx. 76% 16 hours light/day (hatchlings)	EPA requires: temperature of 39°C (102°F) humidity of 70%			
When hatched eggs were removed, counted	Days 27 or 28	EPA : Bobwhite day 24 Mallard day 27			

Parameter	Details	Remarks Criteria
Were egg shells washed and dried for at least 48 hrs before measuring?	Yes, shells were washed and airdried for at least 1 week.	
Egg shell thickness no. of eggs used:	One egg was collected (when available) from each odd numbered cage during odd numbered weeks and from each even numbered cage during the even numbered weeks.	EPA requires newly hatched eggs be collected at least once every two weeks. Thickness of the shell plus membrane should be measured to the nearest 0.01 mm; 3 - 4 measurements per shell.
intervals:	Once weekly throughout the egg laying period.	
mode of measurement:	Five points around the equatorial circumference were measured to the nearest 0.005 mm.	
Reference chemical, if used	None used	

2. Observations:

Table 3: Observations.

Parameter	Remarks/Criteria	
Parameters measured		
Parental:	Mortality, body weight, food consumption, signs of toxicity, necropsy	EPA requires: Eggs laid/pen, Eggs cracked/pen, Eggs set/pen, Viable embryos/pen, Live 3-week embryos/pen, Normal hatchlings/pen,
Egg collection development:	Eggs laid, eggs cracked, eggshell thickness, eggs set, viable embryos, live 3-week embryos, number of hatchlings, hatchling body weight, number of 14-day-old survivors, 14-day-old survivor body weight	14-day-old survivors/pen, 14-day-old survivors/pen, Weights of 14-day-old survivors (mean per pen), Egg shell thickness, Food consumption (mean per pen), Initial and final body weight (mean per pen)
Indicate if the test material was regurgitated	No indications of dietary regurgitation.	

PMRA Submission Number

EPA MRID Number 42867902

Parameter	Details	Remarks/Criteria			
Observation intervals (for various parameters)	Parental and hatchling mortality and signs of toxicity were recorded once daily. Parental body weights were recorded at the start of acclimation, at Weeks 0, 2, 4, 6, 8 and at test termination (Week 22). Parental food consumption was determined weekly.	Body weights and food consumption must be measured at least biweekly.			
Were raw data included?	Yes, sufficient.				

I. RESULTS AND DISCUSSION:

A. MORTALITY:

No treatment-related mortality was observed during the study; however, two incidental mortalities occurred, one each from the control and 175 ppm groups.

The single mortality in the control group was a hen that was found dead during Week 5. The day prior to death, the hen exhibited reduced reaction to external stimuli, lower limb weakness, and shallow and rapid respiration. The bird was thin, with reduced muscle mass. No external lesions were observed. Internally, multiple plaques and lesions which appeared fungal in nature were noted on the lungs, air sacs, and throughout the abdominal cavity. The gizzard was empty and the gizzard lining appeared to be bile-stained. No other lesions were noted, and aside from lesions of bumblefoot, necropsy of the pen-mate was unremarkable.

The single mortality in the 175 ppm group was a drake that was found dead during Week 14. The bird was observed with a slight limp and lesions of bumblefoot during Week 6. The drake appeared normal by the end of Week 7. Lameness and bumblefoot again were noted during Week 11. These effects improved during subsequent weeks, but the animal was noted to be thin. Immediately prior to death, the drake was prostrate with legs extended, with a prominent keel. The bird was thin and appeared to have some loss of muscle mass, extensive lesions of bumblefoot on both feet, and a fecal and urinate-matted vent. Internally, the spleen was greatly enlarged and there was evidence of slight peritonitis and adhesions in the abdominal cavity. Approximately 25 cm of the middle of the small intestines was greatly distended and hemorrhagic, with caseous necrosis and hemorrhagic areas in the gut wall. The testes appeared to be regressing. No other lesions were noted, and necropsy of the pen-mate was unremarkable.

No other mortalities were observed during the study, and due to the nature of lesions observed at necropsy, the single mortality at the 175 ppm level was considered not to be related to treatment.

PMRA Submission Number

EPA MRID Number 42867902

Table 4: Effect of Metaldehyde Technical on Mortality of Anas platyrhynchos.

Treatment, ppm a.i.	Week 7 No. Dead Male Female		Week 14 No. Dead Male Female		No. Dead Male Female	
measured (nominal)						
Control	0	1	0	1	0	1
49 (50)	0	0	0	0	Ó	0
176 (175)	0	0	1	. 0	1	0
497 (500)	0	0	0	0	0	0

B. REPRODUCTIVE AND OTHER ENDPOINTS:

Abnormal Effects/Behavior: Clinical signs that appeared to be treatment related were observed in three hens from the 500 ppm level. In all instances, during a washing procedure when the birds were allowed to bathe in a gentle spray of water, hens were observed to exhibit convulsive behavior at only one time interval. Episodes occurred in single birds during Weeks 12, 19, and 20. In all cases, the hens appeared to recover completely within 15 minutes of the episode and the clinical signs did not re-occur. No other treatment-related clinical signs of toxicity were observed. Incidental clinical observations normally associated with pen wear and/or interactions among pen mates were observed in all test groups and included eye lesions, feather loss, and foot and ankle lesions with resultant lameness. The LOAEC for clinical signs of toxicity in adult birds was 500 ppm.

<u>Food Consumption</u>: Due to excessive feed wastage by some birds, feed consumption was variable between pens. However, no treatment-related effects were observed. Statistically-significant differences from the control group were observed at the 50 ppm level during Week 2, at the 175 ppm level during Week 9, and at the 500 ppm level during Weeks 2, 3, and 17; however, these differences were small and lacked a consistent pattern of change. Overall feed consumption averaged 136 g/bird/day for the control group, compared to 145, 136, and 133 g/bird/day for the 50, 175, and 500 ppm groups, respectively (reviewer-calculated). The LOAEC for food consumption was >500 ppm.

<u>Body Weight</u>: No treatment-related effects on body weight were observed, with no statistically-significant differences between the control and any treatment group at any of the intervals. The LOAEC for adult body weight was >500 ppm.

Necropsy: The study authors noted that the incidence of regressed or regressing ovaries tended to increase with increasing concentration. The reviewer observed that the incidence was clearly increased with regressing ovaries, but the number of fully regressed ovaries was highest at the 50 ppm level, with no regressed ovaries at the 175 or 500 ppm levels. The numbers of regressing ovaries were 6/15, 7/16, 10/15, and 14/16 for the control, 50, 175, and 500 ppm levels, respectively, and the numbers of regressed ovaries were 1/15, 4/16, 0/15, and 0/16, respectively. When combined, the numbers of regressing/regressed ovaries were 7/15, 11/16, 10/15, and 14/16 for the control, 50, 175, and 500 ppm levels, respectively. There were no other findings at necropsy that were related to treatment with Metaldehyde Technical. The LOAEC for post-mortem findings was not reported.

Reproductive Effects: No treatment-related effects were observed on egg production or quality, fertility, embryonic development, hatchability, or survival of hatchlings at the 50 or 175 ppm test levels. At the 50 ppm level, there was a slight, statistically-significant reduction compared to the control group in hatchlings as a

percentage of live 3-week embryos (86 versus 95% for the control group). However, the difference observed was the result of exceptional hatchability in the control group (95 \pm 4% compared to a historical control value of 70 \pm 10%). Furthermore, the hatchability at the 50 ppm level (86 \pm 10%) was also above the historical control value, and no statistical difference was observed at the next higher treatment level of 175 ppm. Therefore, this difference was not considered to be related to treatment.

At the 500 ppm level, treatment-related effects on egg production, egg quality (thickness), hatching success, survival of hatchlings, and consequently overall hatching success (measured as the number of 14-day old survivors/hen, 17 versus 34 for the control) were observed. While the reduction in egg production (percentage of eggs laid of maximum laid) was not statistically-different from the control (40 versus 58%), it appeared to be the result of a decrease in the number of hens laying a high number (>50) of eggs, and the effect was most notable during the latter portion of the egg production period. Egg quality was also affected at this level, with a statistically-significant reduction compared to the control in mean egg shell thickness (0 350 versus 0.378 mm). The reductions in hatching success and hatchling survival were evident in statistically-significant reductions compared to the control in the percentage of hatchlings of 3-week embryos (80 versus 95%) and the percentage of 14-day old survivors of hatchlings (88 versus 99%). The effects were further reflected in statistically-significant reductions in the percentage of hatchlings of eggs set (64 versus 85%), the percentage of 14-day old survivors of eggs set (56 versus 84%), the percentage of hatchlings of maximum eggs set (27 versus 50%), and the percentage of 14-day old survivors of maximum eggs set (24 versus 49%).

No overt signs of toxicity were observed in hatchlings from the control, 50, or 175 ppm levels, and no treatment-related effect on offspring body weights were observed at any treatment level. Offspring from the 500 ppm level displayed profound clinical signs that appeared to be treatment related. In general, up to approximately one-third of the offspring hatched in any given week displayed dorsal or ventral neck curl, and circling behavior. Furthermore, the ducklings from this level appeared more excitable and disoriented than normal offspring. In a number of cases, the ducklings that survived appeared to improve as they matured. The LOAEC for effects on reproduction was 500 ppm.

Table 5: Reproductive and other parameters (nominal concentrations; study author-reported).

Parameter	Control	50 ppm	175 ppm	500 ppm	NOAEC	LOAEC
Eggs laid	682	750	682	511	N/A	N/A
Eggs laid/hen	45	47	45	32	N/A	N/A
Eggs laid/hen/day	0.52	0.54	0.52	0.37	N/A	N/A
Eggs laid/maximum laid (%)	58	59	58	40*	175 ppm	500 ppm
Eggs cracked	20	15	8	22	N/A	N/A
Eggs cracked/eggs laid (%)	3	2	1	4	500 ppm	>500 ppm
Shell thickness (mm ± SD)	0.378 ± 0.027	0.381 ± 0.033	0.375 ± 0.026	0.350 ± 0.030*	175 ppm	500 ppm
Eggs set	590	659	599	434	N/A	N/A
Viable embryos	552	533	480	371	N/A	N/A
Viable embryos/eggs set (%)	90	78	80	81	500 ppm	>500 ppm
Live 3-week embryos	550	525	475	366	N/A	N/A
Live 3-week embryos/viable embryos (%)	100	98	99	99	500 ppm	>500 ppm
No. of hatchlings	519	457	422	296	N/A	N/A

EPA MRID Number 42867902

Parameter	Control	50 ppm	175 ppm	500 ppm	NOAEC	LOAEC
No. of hatchlings/live 3-week embryos (%)	95	86*	89	80**	175 ppm	500 ppm
No. of hatchlings/eggs set (%)	85	66	71	64*	175 ppm	500 ppm
Hatchling weight (g ± SD)	33 ± 3	34 ± 3	34 ± 3	33 ± 3	500 ppm	>500 ppm
No. of 14-day old survivors	511	454	414	265	N/A	N/A
No. of 14-day old survivors/hen	34	28	28	17	N/A	N/A
No. of 14-day old survivors/No. of hatchlings (%)	99	99	98	88**	175 ppm	500 ppm
No. of 14-day old survivors/eggs set (%)	84	66	70	56**	175 ppm	500 ppm
14-day old survivors weight ($g \pm SD$)	298 ± 35	297 ± 32	284 ± 41	274 ± 37	500 ppm	>500 ppm
Mean adult food consumption (g/pen/day) ¹	136	145	136	133	500 ppm	>500 ppm
Weight of adult males, g at start of treatment: at Week 8: at Week 22 (study termination):	1216 1188 1201	1232 1161 1196	1219 1162 1222	1235 1184 1219	500 ppm	>500 ppm
Weight of adult females, g at start of treatment: at Week 8: at Week 22 (study termination):	1087 1077 1128	1075 1031 1090	1064 1050 1127	1067 1091 1104	500 ppm	>500 ppm
Gross pathology Ovary Regressing Ovary Regressed	6/15 1/15	7/16 4/16	10/15 0/15	14/16 0/16		Not reported

N/A = Not statistically-analyzed.

C. REPORTED STATISTICS:

The following variables were statistically analyzed: adult body weight, adult feed consumption, eggs laid of maximum laid, eggs cracked of eggs laid, viable embryos of eggs set, live 3-week embryos of viable embryos, hatchlings of 3-week embryos, 14-day old survivors of hatchlings of eggs set, 14-day old survivors of eggs set, hatchlings of maximum set, 14-day old survivors of maximum set, egg shell thickness, and offspring's body weight.

An analysis of variance (ANOVA) was performed to determine statistically-significant differences between groups. Dunnett's multiple comparison procedure was then used to compare the treatment means with the control group mean. Sample units were the individual pens within each experimental group, except adult body weights, where the sample unit was the individual bird. Percentage data were examined using Dunnett's method following arcsine square root transformation. Nominal concentrations were used for all estimations.

^{*} Significantly different from the control at p<0.05.

^{**} Significantly different from the control at p<0.01.

¹ Reviewer-calculated from mean weekly data.

D. VERIFICATION OF STATISTICAL RESULTS:

Statistical Method: Analysis was conducted using "chicks.sas" (Ver. 3; March 2002), a SAS program provided by EFED/OPP/USEPA. Data for all endpoints were examined graphically using box plots to determine if they exhibited a dose-dependent response, which was ultimately used to select the multiple comparison test to detect LOAEC and NOAEC. Data for each endpoint were tested to determine if their distributions were normal and if their variances were homogeneous using Shapiro-Wilk's and Levene's tests, respectively. Data that satisfied these assumptions were subjected to Dunnett's and William's tests and data that did not satisfy these assumptions were subjected to the non-parametric MannWhitney-U (with a Bonferroni adjustment) and Jonckheere's tests. Data for dead birds were excluded from the analyses. See Appendix I for output of reviewer's statistical verification and graphs for affected endpoints to support any reviewer-generated conclusions that may differ from those reported in the study.

Table 6. Reproductive and other parameters (mean-measured concentrations; reviewer-reported).

Parameter	Control	49 ppm	176 ppm	497 ppm	NOAEC	LOAEC
Eggs laid/pen	45	47	45	32	497 ppm	>497 ppm
Eggs cracked/pen	1.3	0.9	0.5	1.4	497 ppm	>497 ppm
Eggs not cracked/eggs laid (%)	96.8	98.1	98.7	95.5	497 ppm	>497 ppm
Eggs set/pen	39.3	41.2	39.9	27.1*	176 ppm	497 ppm
Shell thickness	0.35	0.38	0.37	0.35	497 ppm	>497 ppm
Eggs set/eggs laid (%)	85.7	87.9	87.6	82.4	497 ppm	>497 ppm
Viable embryo/pen	36.8	33.3	32.0	23.2	497 ppm	>497 ppm
Viable embryos/eggs set (%)	90.5	77.6	80.2	80,6	497 ppm	>497 ppm
Live embryos/pen	36.7	32.8	31.7	22.9	497 ppm	>497 ppm
Live embryo/viable embryo (%)	99.7	98.3	99.1	98.9	497 ppm	>497 ppm
No. of hatchlings/pen	34.6	28.6	28.1	18.5*	176 ppm	497 ppm
No. of hatchlings/eggs laid (%)	73.9	57.9*	62.6*	54.4*	<49 ppm	49 ppm
No. of hatchlings/eggs set (%)	85,4	65.9*	71.1*	63.5*	<49 ppm	49 ppm
No. of hatchlings/live embryos (%)	94.9	86.1*	89.3*	80.2*	<49 ppm	49 ppm
Hatchling survival/pen	34.1	28.4	27.6	16.6*	176 ppm	497 ppm
Hatchling survival/eggs set (%)	. 84.3	65.5*	69.7	55.8*	<49 ppm	49 ppm
Hatchling survival/no. of hatchlings (%)	98.8	99.5	98.1	88.0*	176 ppm	497 ppm
Hatchling weight (g)	30.4	29.2	31.4	28.8	497 ppm	>497 ppm
Survivor weight (g)	277.1	256.3	259.1	234.2	497 ppm	>497 ppm
Mean food consumption (g/bird/day)	135.7	145.1	136.4	133.6	497 ppm	>497 ppm
Male weight gain (g)	-6.5	-36.5	7.6	-16.6	497 ppm	>497 ppm
Female weight gain (g)	104.7	14.5	59.4	36.8	497 ppm	>497 ppm

^{*} Significantly different from the control at p<0.05.

E. STUDY DEFICIENCIES: There were no significant deviations from U.S. EPA guide line §71-4(b) that affected the validity or acceptability of this study.

F. REVIEWER'S COMMENTS:

Results of the reviewer's statistical analysis differed slightly from those of the study authors. The reviewer's analysis detected greater sensitivity of some reproductive endpoints (*i.e.*, number hatched to eggs set, number hatched to live embryos, hatchling survival to eggs set); the study authors concluded that differences were significant only at the highest treatment level, while the reviewer's analysis detected significant reductions at all treatment levels (ratios of number hatched to eggs set and number hatched to live embryos) or at the lowest treatment level (hatchling survival to eggs set). In addition, the reviewer's analysis detected significant effects on several endpoints that were not statistically analyzed by the study authors, including eggs set, number hatched, ratio of number hatched to eggs laid, and hatchling survival. The reviewer's results are based on the mean measured concentrations and are reported in the Conclusions and Executive Summary sections.

G. CONCLUSIONS:

This study is scientifically sound, but it does not fulfill the guideline requirements for a reproductive toxicity study with Mallard duck (§71-4b) because a NOAEC could not be identified. As a result, this study is classified as Supplemental.

NOAEC: <49 ppm a.i. LOAEC: 49 ppm a.i.

Endpoint(s) Affected: Clinical signs of toxicity (adults and offspring), eggs set, number hatched, ratio of number hatched to eggs laid, number hatched to eggs set, number hatched to live embryos, hatchling survival, ratio of hatchling survival to eggs set, and hatchling survival to number hatched.

III. REFERENCES:

- American Society for Testing and Materials. 1986. Standard Practice for Conducting Reproductive Studies with Avian Species. E1062-86. Philadelphia, PA. 15 pp.
- U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, FIFRA Subdivision E, Hazard Evaluation: Wildlife and Aquatic Organisms, Subsection 71-4. Environmental Protection Agency, Office of Pesticide Programs, October, 1982.

National Institute of Health. 1985. Guide for the Care and Use of Laboratory Animals. Pub. No. 85-23. 83 pp.

Dunnett, C.W. 1955. A Multiple Comparisons Procedure for Comparing Several Treatments with a Control. Jour. Amer. Statis. Assoc. 50: 1096-1121.

Dunnett, C.W. 1964. New Tables for Multiple Comparisons with a Control. Biometrics 20: 482-491.

APPENDIX I. OUTPUT OF REVIEWER'S STATISTICAL VERIFICATION:														
Μá	allard :	repro	, I	Metaldeh	/de,	MRID 42	28679	02						
PI	RINTOUT	OF R	WAS											
	s TRT	EL E		ENC_EL	ES	ES_EL	VE	VE_ES	LE	$\text{LE}_{ ext{VE}}$	NH	NH EL	NH ES	
1	Ctrl	31	1	96.77	2.6	83.87	26	100.00	26	100.00	26	83.87	100.00	
2	Ctrl	45	2	95.56	37	82.22	35	94.59	35	100.00	35	77.78	94.59	
3	Ctrl	22	0	100.00	20	90.91	18	9.0.00	18	100.00	16	72.73	80.00	
4	Ctrl	58	0	100.00	51	87.93	47	92.16	45	95.74	43	74.14	84.31	
5	Ctrl	68	3	95.59	59	86.76	58	98.31	58	100.00	51	75.00	86.44	
6.	Ctrl	. 69	0	100.00	62	89.86	55	88.71	55	100.00	54	78.26	87.10	
7	Ctrl	66	2	96.97	56	84.85	52	92.86	52	100.00	49	74.24	87.50	
8	Ctrl	20	3	85.00	13	65.00	5	38.46	5	100.00	. 5	25.00	38.46	
9	Ctrl	0	0	•	0		. 0		Ō		0			
10) Ctrl					٠.								
11	Ctrl	60	1	98.33	52	86.67	50	96.15	50	100.00	47	78.33	90.38	
12	Ctrl	79	3	96.20	69	87.34	67	97.10	67	100.00	63	79.75	91.30	
13		56	3	94.64	48	85.71	47	97.92	47	100.00	41	73.21	85.42	
14	Ctrl	50	1	98.00		90.00	44	97.78	44	100.00	43	86.00	95.56	
15		19	0	100.00	17	89.47	15	88.24	15	100.00	$\frac{13}{14}$	73.68	82.35	
16		39	- 1	97.44	35	89.74	33	94.29	33	100.00	32	82.05	91.43	
17			1	98.15	47		45	95.74	44	97.78	42	77.78	89.36	
18				100.00	34	89.47	33	97.06	32	96.97	25	65.79	73.53	
19			1	97.87	39	82.98	. 0	0.00	0	90.97	23	0.00	0.00	
20			1	97.62	37	88.10	26	70.27	26	100.00				
21			0	100.00	21	87.50	17	80.95	17	100.00	24	57.14	64.86	
22			Ö	100.00	23	×92.00	10	43.48	9	90.00	10	41.67	47.62	
23			2	96.88	5.3	82.81	51	96.23			. 8	32.00	34.78	
24			0	100.00	45	90.00	45		51	100.00	48	75.00	90.57	
25			1	97.30	33	89.19		100.00	45	100.00	35	70.00	77.78	
2.6			Ō	100.00		89.47	11	0.00	0	100.00	0	0.00	0.00	
27			1	97.56	51		41	80.39	41	100.00	38	66.67	74.51	
28					37	90.24	35	94.59	35	100.00	33	80.49	89.19	
29			0	100.00	27	90.00	27	100.00		100.00	22	73.33	81.48	
30			1	98.61	65	90.28	64	98.46	63	98.44	58	80.56	89.23	
31			2	92.86	23	82.14	22	95.65	22	100.00	21	75.00	91.30	
			1	98.63	66	90.41	64	96.97	61	95.31	51	69.86	77.27	
3:2			4	94.12	58	85.29	53	91.38	52	98.11	42	61.76	72.41	
33			1	98.21	48	85.71	46	95.83	45	97.83	45	80.36	93.75	١.
34			0	100.00	27	79.41	21	77.78	21	100.00	17	50.00	62.96	
35	7.4		0	100.00	45	81.82	29	64.44	29	100.00	24	43.64	53.33	
36			0.	100.00	50	92.59	50	100.00	50	100.00	46	85.19	92.00	
37			1	98.41	56	88.89	53	94.64	52	98.11	40	63.49	71.43	
38			0	100.00	24	88,89	23	95.83	23	100.00	23	85.19	95.83	
39			1	97.83	39	84.78	0	0.00	0		0	0.00	0.00	
40			0	100.00	42	91.30	30	71.43	30	100.00	26	56.52	61.90	
41			0	100.00	34	89.47	33	97.06	33	100.00	32	84.21	94.12	
42			0	100.00	33	86.84	33	100.00	32	96.97	27	71.05	81.82	
43			• .	•	•		. •		•	•	•	•	•	
44			1	96.88	29	90.63	29	100.00	29	100.00	26	81.25	89.66	
45			1	96.97	28	84.85	24	85.71	23	95.83	20	60.61	71.43	
46			2	93.55	27	87.10	17	62.96	17	100.00	17	54.84	62.96	
47			0	100.00	59	92.19	38	64.41	38	100.00	32	50.00	54.24	
48			1	98.46	58	89.23	54	93.10	53	98.15	47	72.31	81.03	
49			0	100.00	24	88.89	22	91.67	22	100.00	15	55.56	62.50	
50			2	93.10	24	82.76	24	100.00	24	100.00	21	72.41	87.50	
51			1	98.41	55	87.30	50	90.91	49	98.00	35	55.56	63.64	
52			3	90.63	26	81.25	25	96.15	24	96.00	22	68.75	84.62	
53			7	90.41	60	82.19	53	88.33	51	96.23	44	60.27	73.33	
54		3 22	0 .		19	86.36	19	100.00	19	100.00	7	31.82	36.84	
55		3 48	2	95.83	40	83.33	26	65.00	26	100.00	24	50.00	60.00	
56			1	95.00	17	85.00	16	94.12	15	93.75	12	60.00	70.59	
57	Dose3	6	1	83.33	2	33.33	0	0.00	0	•	. 0	0.00	0.00	

1 1/11	CA BUUL	11122101	II TAN	moer								EP	A MIKID N	umber 42	00/9
			_						_					* , *	
58	Dose3			100.		93.33	27		5.43	27	100				
59 60	Dose3 Dose3		1	94.		76.47	11		1.62	11	100			69.23	
61	Dose3		1	96. 93.		88.46	0		0.00	.0	100	. 0		0.00	
62	Dose3			100.		84.85 85.71	25		2.29	25	100.		63.64	75.00	
63	Dose3		1	97.		85.71	18 29		0.00 5.67	18 29	100.			77.78	
64	Dose3			100.		93.10	26		5.30	26	100.			76.67 96.30	
			Me	tald	lehyde, 1			an2		20	100.	.00 26	09.00	90.30	
					(contin		507.	702			:		-		
	TRT	NH I		HS	HS ES		TI T	HICK F	IATWT	SUR	VWT	FOOD	WTGAINM	WTGAINE	•
1	Ctrl	$10\overline{0}$.	00	26	100.00	100.0		0.36	35		70	111	-45	87	
2	Ctrl	100.	00	34	91.89	97.1	4	0.39	31		87	112	-68	98	
3	Ctrl	88.		16	80.00	100.0)	0.36	34	: 3	16	112	114	71	
4	Ctrl	95.		42	82.35	97.6		0.41	34		76	123	62	99	
5 .	Ctrl	87.		4 9	83.05	96.0		0.40	30		75	158	24	166	
6	Ctrl	98.		50	80.65	92.5	9	0.38	33		00	133	35	-39	
.7	Ctrl	94.		49	87.50	100.0		0.38	36		46	178	-106	1007	
8	Ctrl	100.	.00	5	38.46	100.0		0.35	34	2	76	100	-152	95	
9	Ctrl	•		0 .	•	. •		0.00	0		0	141	31	-93	
10	Ctrl Ctrl	٠.	00	47		100 0	_			_	•			_:	
$\frac{11}{12}$	Ctrl	94. 94.		47 63	90.38 91.30	100.00		0.35	32		05	126	10	55 13	
13	Ctrl	87.		41	85.42	100.00		0.37 0.37	32		04	199	-87	13	
14	Ctrl	97.		43	95.56	100.0		0.37	33 · 30		07 66	110 149	46 -24	-69°	
15	Ctrl	93.		$\frac{43}{14}$	82.35	100.0		0.45	30		12	149		-16 -26	
16	Ctrl	96.		32	91.43			0.38	32		16	135	- - 9 72	123	
17	Dose1			42	89.36	100.00		0.35	32		67	164	-108	44	
18	Dose1	78.		25	73.53	100.00		0.37	38		19	138	57	97	
19	Dose1			0	0.00			0.38	0	Ŭ.	0	125	-35	84	
20	Dose1	92.		24	64.86	100.00		0.35	32	3	00	131	-218	. 23	
21	Dose1	58.		10	47.62	100.00		0.34	31		36	156	16	7	
22	Dose1	88.	89	8	34.78	100.00		0.35	31		85	140	43	-182	
23	Dose1	94.		48	90.57	100.00)	0.38	34	3	12	129	-107	17	
24	Dose1	77.	78	34	75.56	97.1	4	0.43	38	3	17	143	-99	-28	
25	Dose1			√ 0	0.00			0.38	0		0	139	-149	-8	
26	Dose1	92.		37	72.55	97.3		0.37	33		93	137	.69	-5	
27	Dose1	94.		33	89.19	100.00		0.38	33		80	158	195	-10	
28	Dose1	81.		22	81.48	100.00		0.37	33		80	127	-199	-40	
29	Dose1	92.		58	89.23	100.00		0.39	33		06	111	-1	62	
30 31	Dose1 Dose1	95. 83.		21 50	91.30 75.76	100.00		0.43	33		94	142	-108	-105	
32	Dose1	80:		42	72.41	100.00		0.36			80 32	195	7 53	52	
33	Dose2			45	93.75	100.00		0.40	36 36		32 78	186 128	71	224 78	
34	Dose2	80.		17	62.96	100.00		0.37	32		80	115	68	19 <u>6</u>	
35	Dose2	82.		24	53.33	100.00		0.38	34		81	126	72	185	
36	Dose2	92.		46	92.00	100.00		0.39	37		02	123	-18	56	
-37	Dose2	76.		40	71.43	100.00		0.39	34		90	142	88	40	
38	Dose2	100.	00	22	91.67	95.65		0.37	32		05	130	85	-44	
39	Dose2			. 0	0.00			0.38	0		0	154	-9	9	
40	Dose2		67	24	57.14	92.33	L	0.38	32	2	55	117	74	-84	
41	Dose2			32	94.12	100.00		0.34	33	3	29	123	-85	-4	
42	Dose2	84.	38	26	78.79	96.30) .	0.40	33	3	07	147	12	42	
43	Dose2					•		0.34	•			•	-	•	
44	Dose2	89.		25	86.21	96.15			35		91	133	-3	-19	
45	Dose2	86.		20	71.43	100.00		0.33	34		59	150	12	120	
46 47	Dose2 Dose2	84.		.17	62.96	100.00		0.37	35		03	136	-21	198	
4 7	Dose2	88.		31 45	52.54 77.59	96.88 95.74		0.37	29		23	142	-191	97	
49	Dose3	68.		15	62.50	100.00		0.37	35 31		84	180	-41 106	21	
50.	Dose3	87.		20	83.33	95.24		0.39	31		87 64	118 122	106 112	-147	
51	Dose3	71.		31	56.36	88.57		0.37	35		76	171	112	25 301	
52	Dose3	91.		20	76.92	90.91		0.36	. 28		76	130	-88	-155	
										_	. •		٥٢	100	

platyrhynchos		•		
PMRA Submission Number			EPA	MRID Number 42867902
				
FO - O O O O O O O O O O O O O O O O O O				. 1
53 Dose3 86.27 44	73.33 100.00	0.36 35	302 130	-39 216
54 Dose3 36.84 7	36.84 100.00	0.39 34	302 116	116 -18
55 Dose3 92.31 22	55.00 91.67	0.34 32	270 125	2 127
56 Dose3 80.00 12	70.59 100.00	0.32 31	244 102	-249 -121
57 Dose3 . 0	0.00	0.31 0	0 122	-175- 4
58 Dose3 85.19 22	78.57 95.65	0.37 33	274 145	-87 -15
59 Dose3 81.82 4	30.77 44.44	0.26 33	203 120	4 93
60 Dose3 . 0	0.00	0.37 0	0 - 159	40 13
61 Dose3 84.00 14	50.00 66.67	0.36 34	222 169	78 –36
62 Dose3 77.78 13	72.22 92.86	0.35 31	293 130	52 19
63 Dose3 79.31 17	56.67 73.91	0.36 37	279 127	-24 131
64 Dose3 100.00 24		0.35 32	255 152	-131 151
04 Doses 100.00 24	92.31	0.33 32	233 132	_131 131
25:22	1 1 10055			*
Mallard repro, Metald	enyde, MRID 42867	902		
ANALYSIS RESULTS FOR	VARIABLE EL (Eg	gs Laid)		
		$(A_{ij}, A_{ij}, A_{$		
TESTS OF ASSUMPTIONS	FOR PARAMETRIC AND	ALYSIS		
Shapiro-Wilks test fo			0	
Levenes test for homo	consitu of marine	siduais ai	ond rever-0.01	nh
Levelles cest for nomo	genercy or variant	ce (absorate re	esiduais) ai	pna-rever=0.05
Use parametric analys				rametric analyses.
Shapiro-Wilks Shap			s Conclusion	
Test Stat P-	value Test:	Stat P-value	e in the second	
0.989 0	.852 1.9	62 0.130	USE PARAMET	RIC TESTS
*****	*****	*****	*****	***
BASIC SUMMARY STATIST				
Level N Mean	StdDev StdE			f.Interval
Ctrl 15 45.47	22.88 5.9	1 50.31	32.80	, 58.13
Dose1 16 46.88	16.52 4.1	3 35.24	38.07	, 55.68
Dose2 15 45.47	13.20 3.4		38.16	
Dose3 16 31.94	16.85 4.2		22.96	
D0505 10 51.54	10.00	1 32.73	22.90	, 40.91
T 1	3.01			
Level Median	Min Max	%of Control	l(means) %Red	uction(means)
Ctrl 50.00	0.00 79.0	0 ,		• •
Dose1 44.50	24.00 73.0	0 103.10	· -	3.10
Dose2 46.00	27.00 65.00	0 100.00		0.00
Dose3 29.00	6.00 73.0			9.76
23.00	75.0	70.21	2	5.70
******	والمراور والمراب بالمراور والمرابط والمرابط والمرابط والمرابط والمرابط والمرابط	An almaha da almaha d		

PARAMETRIC ANALYSES	- use alpha-leve	el=0.05 for al	ll tests	
Analysis of Varia	nce (ANOVA) - ove:	rall F-test		* · · · · · · · · · · · · · · · · · · ·
	Denominator df	F-stat	P-value	
3	58	2.51	0.067	
		2.01	0.007	
Divini and the man				
Dunnett - testing each	n trt mean signif	. less than co	ontrol	
Williams - test assum	es dose-response :	relationship,	testing negati	ve trend
Tukey - two-sided tes	ts, all possible of	comparisons, r	not used for NO	AEC or LOAEC
Level Mean Dunne	tt Isotonic Wil	liams	Tukou	p-values
p-val:	ue mean p-	value Dosel	Dose2 Dose	3 Dose4 Dose5
Ctrl 45.47 .	46.19	0.996	1.000 0.15	6
Dosel 46.88 0.82	1 46.19 0	.632 .	0.996 0.09	
Dose2 45.47 0.74		.618	0.15	
Dose3 31.94 0.04			. 0.13	•
50365 51.94 0.04	, 51.94 0	.023	•	•
CID OCT DY-				
SUMMARY	NOAEC	LOAEC		
Dunnett	Dose2	Dose3		
Williams	Dose2	Dose3	,	
•		3-4-30		."

PMRA Submission Number

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE NEG_EC (Eggs Cracked)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion
Test Stat	P-value	Test Stat	P-value	
0.842	<.001	1.759	0.165	USE NON-PARAMETRIC TESTS

*****	***	****	******	*****	*****	*****	*****	ł-
BASIC ST	AMMU	RY STATIS	TICS					
Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Ir	iterval	
Ctrl	15	1.33	1.23	0.32	92.58	0.65,	2.02	
Dose1	16	0.94	1.06	0.27	113.35	0.37,	1.50	
Dose2	15	0.53	0.64	0.17	119.99	0.18,	0.89	
Dose3	16	1.38	1.75	0.44	127.01	0.44,	2.31	
						() () () ()		
Level		Median	Min	Max	%of Control (means)	%Reducti	on(means)	
Ctrl		1.00	0.00	3.00				
Dose1		1.00	0.00	4.00	70.31	29.69	,	*
Dose2		0.00	0.00	2.00	40.00	60.00		
Dose3		1.00	0.00	7.00	103.13	-3.13		

Kruskal-Wallis test - equality among treatment groups
Degrees of Freedom TestStat P-value

Degrees of Freedom TestStat P-value 4.19 0.241

MannWhit(Bon) - testing each trt median signif. greater than control Jonckheere - test assumes dose-response relationship, testing positive trend

	Median	Ma nnW	hit(Bon	adjust)p-	value	Jonckheere	p-value
Ctrl	1.00			•	•		·
Dosel	1.00			1.000		0.80	. 8
Dose2	0.00			1.000		0.96	9
Dose3	1.00			1.000		0.69	2
SUMMARY			NOAEC		LOAEC		
MannWhit	(Bonf	adjust)	Dose3		>highest	dose	

>highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE ENC EL ((EL-EC)/EL (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.856 <.001 2.916 0.042 USE NON-PARAMETRIC TESTS BASIC SUMMARY STATISTICS Level N 95% Conf.Interval Mean StdDev StdErr Coef of Var 3.85 2.13 1.84 1.03 3.98 Ctrl 14 96.75 94.53, 2.17 0.53 Dosel 16 96.96, 98.10 99.24 Dose2 15 0.48 97.67, 98.69 1.87 99.71 Dose3, 16 4.63 4.84 95.50 97.97 1.1693.04, Max %of Control (means) %Reduction (means) Level Median Min 85.00 100.00 92.86 100.00 Ctrl 97.20 Dose1 98.38 101.39 -1.39100.00 102.00 Dose2 93.55 100.00 -2.00Dose3 95.99 83.33 100.00 98.71 1.29 ************************************* NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 6.71 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value 97.20 Ctrl Dose1 98.38 1.000 0.882 Dose2 100.00 1.000 0.974 Dose3 95.99 0.627 0.375

Doses	33.33	0.02	
SUMMARY MannWhit Jonckheer	(Bonf adjust) re	NOAEC Dose3 Dose3	LOAEC >highest dose >highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE ES (Eggs Set)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

-	t Stat .991	-	-value 0.926	Test Stat 2.136	P-value 0.105	USE PARAMETRIC	TESTS
*****	****	****	******	*****	*****	*****	*****
BASIC ST	J M MARY	STATIS:	rics				
Level	N	Mean	StdDev	StdErr	Coef of Va	r 95% Conf.I	nterval
Ctrl	15	39.33	20.31	5.25	51.65	28.08,	50.58
Dose1	16	41.19	14.56	3.64	35.34	33.43,	48.94
Dose2	15	39.93	12.19	3.15	30.52	33.19,	46.68
Dose3	16	27.13	14.50	3.63	53.46	19.40,	34.85

Median %of Control (means) Level Min Max %Reduction (means) Ctrl 45.00 0.00 69.00 104.71 Dose1 38.00 21.00 66.00 -4.7139.00 ,24.00 Dose2 101.53 59.00 -1.5325.00 2.00 60.00 68.96 31.04

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test

Numerator df Denominator df F-stat P-value 3 58 2.79 0.048

Dunnett - testing each trt mean signif. less than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p-v Dose3	values Dose4	Dose5
Ctrl	39.33		40.29	•	0.987	1.000	0.143		
Dose1	41.19	0.851	40.29	0.654	*	0.996	0.064		
Dose2	39.93	0.784	39.93	0.663		•	0.115		
Dose3	27.13	0.043	27.13	0.020		•			•

SUMMARY	NOAEC	LOAEC
Dunnett	Dose2	Dose3
Williams	Dose2	Dose3

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE ES EL (EggsSet/EggsLaid (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha+level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat Test Stat P-value P-value 0.596 < .001 1.517 0.220 USE NON-PARAMETRIC TESTS ************************************ BASIC SUMMARY STATISTICS Mean StdDev Level N StdErr Coef of Var 95% Conf.Interval Ctrl 14 85.74 6.49
Dosel 16 87.93 3.06
Dosel 15 87.58 3.77
Dosel 16 82.38 13.74 85.74 7.57 1.73 81.99, 89.49 3.48 4.30 86.30, 0.77 89.56 0.97 85.49, 89.67 3.44 16.68 75.06, 89.70 Median Max %of Control (means) Level Min %Reduction(means) Ctrl 87.05 65.00 90.91 82.14 102.56 -2.56Dose1 89.33 92.00 79.41 102.15 88.89 Dose2 92.59 -2.15Dose3 85.36 33.33 93.33 96.08 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 5.08 0.166 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon adjust)p-value	Jonckheere p-value
Ctrl	87.05	· · · · · · · · · · · · · · · · · · ·	
Dose1	89.33	1.000	0.869
Dose2	88.89	1.000	0.751
Dose3	85.36	0.333	0.119
SUMMARY		NOAEC LOAEC	

UMMARYNOAECLOAECMannWhit (Bonf adjust)Dose3>highest doseJonckheereDose3>highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE VE (Viable Embryo(d14))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS
Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion	
Test Stat	P-value	Test Stat	P-value		
0.977	0.293	2.030	0.120	USE PARAMETRIC	TESTS

BASIC SU	JMMARY	STATIS	TICS				
Level	N	Mean	StdDev	StdErr	Coef of Va	r 95% Conf.Ir	nterval
Ctrl	15	36.80	20.15	5.20	54.77	25.64.	47.96
Dose1	16	33.31	20.28	5.07	60.88	22.51,	44.12
Dose2	15	32.00	14.69	3.79	45.90	23.87,	40.13
Dose3	16	23.19	14.14	3.54	60.99	15.65,	30.72
Level		Median	Min	Max	%of Control(m	eans) %Reducti	on(means)
Ctrl		44.00	0.00	67.00		•	
Dose1		34.00	0.00	64.00	90.52	9.48	}
Dose2	1, 1	30.00	0.00	54.00	86.96	13.04	1
Dose3		24.50	0.00	53.00	63.01	36.99	· ·
						· ·	

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test

Numerator df Denominator df F-stat P-value 3 58 1.71 0.176

Dunnett - testing each trt mean signif. less than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOAEC or LOAEC

Level	Mean	Dunnett	Isotonic	Williams ,			Tukey p-v	1 .	_
		p-value	mean	p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	36.80		36.80	•	0.945	0.877	0.148		. <u>.</u>
Dose1	33.31	0.516	33.31	0.348	•	0.997	0.369		
Dose2	32.00	0.429	32.00	0.292	•	•	0.507		_
Dose3	23.19	0.044	23.19	0.021	•	•			•
SUMMAR			NOAEC		LOAEC			- A - A	
Dunne			Dose	2	Dose3				
Will	iams		Dose	2	Dose3		*		

PMRA Submission Number

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE VE ES (ViableEmbryo/EggsSet (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance(absolute residuals) -- alpha+level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value <.001 0.688 2.002 0.124 USE NON-PARAMETRIC TESTS **************** BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval 15.42 33.62 26.27 4.12 Ctrl 14 90.47 17.04 81.57, 99.37 8.40 59.66, Dosel 16 77.57 43.34 95.49 Dose2 15 80.21 6.78 32.75 65.66, 94.76 80.59 32.58 Dose3 16 97.95 8.15 40.43 63.23, Level Median Min Max %of Control(means) %Reduction (means) Ctrl 94.44 38.46 100.00 0.00 85.75 14.25 Dose1 95.12 100.00 0.00 Dose2 93.10 100.00 88.67 11.33 Dose3 92.89 0.00 100.00 89.08 10.92 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 0.81 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value 94.44 Ctrl 1.000 0.287 Dose1 95.12 Dose2 93.10 0.620 0.223 0.826 Dose3 92.89 0.316 SUMMARY NOAEC LOAEC MannWhit (Bonf adjust) Dose3 >highest dose

Dose3

>highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE LE (Live Embryo(d21))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion

Ţ	Cest Stat 0.977	_	-value 0.286	Test Stat 2.104	P-value 0.110	USE	PARAMETRIC	TESTS
				*****	*****	****	****	*****
BASIC	SUMMARY	STATIS	TICS		+ + + + + + + + + + + + + + + + + + + +			
Leve	≥1 N	Mean	StdDev	StdErr	Coef of Va	r	95% Conf.In	iterval
Ctr	rl 15	36.67	20.09	5.19	54.79		25.54.	47.79

Level N	N Mean	StdDev	StdErr	Coef of Var	95% Conf.Ir	iterval
Ctrl 1	15 36.67	20.09	5.19	54.79	25.54,	47.79
Dosel 1	16 32.81	19.86	4.97	60.54	22.23,	43.40
Dose2	15 31.67	14.45	3.73	45.63	23.66,	39.67
Dose3	L6 22.88	13.77	3.44	60.19	15.54,	30.21
Level	Median	Min	Max	%of Control(means)	%Reducti	on(means)
Ctrl	44.00	0.00	67.00	•	•	1 1
Dose1	33.50	0.00	63.00	89.49	10.51	n de la companya de La companya de la co
Dose2	30.00	0.00	53.00	86.36	13.64	1
Dose3	24.00	0.00	51.00	62.39	37.61	

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Analysis of Variance (ANOVA) - overall F-test

Numerator df Denominator df F-stat P-value 3 58 1.78 0.161

Dunnett - testing each trt mean signif. less than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOAEC or LOAEC

Level	Mean	Dunnett	Isotonic	Williams			Tukey p-v	alues	
		p-value	mean	p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	36.67		36.67	•	0.925	0.858	0.130		
Dose1	32.81	0.486	32.81	0.321	•	0.998	0.372		•
Dose2	31.67	0.410	31.67	0.276	•		0.495		
Dose3	22.88	0.039	22.88	0.018		• /	•		•
	RY nett Liams		NOAEC Dose2 Dose2	-	LOAEC Dose3 Dose3				

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE LE VE (LiveEmbryo/ViableEmbryo (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance(absolute residuals) -- alpha+level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat Test Stat P-value P-value 0.750 <.001 2.934 0.042 USE NON-PARAMETRIC TESTS ******************************** BASIC SUMMARY STATISTICS Mean StdDev StdErr 95% Conf.Interval Level N Coef of Var Ctrl 14 Dose1 14 99.70 1.14 0.30 1.14 100.00 99.04, 2.86 98.33 2.82 0.75 96.70, 99.95 1.41 Dose2 14 99.06 0.38 1.43 98.25, 99.88 Dose3 14 98.86 2.06 0.55 2.08 97.67, 100.00 Level Median Min %of Control(means) %Reduction(means) Max Ctrl 100.00 95.74 100.00 98.63 100.00 90.00 1.37 Dose1 100.00 0.63 Dose2 100.00 95.83 99.37 100.00 0.84 Dose3 100.00 93.75 99.16 100.00 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups P-value Degrees of Freedom TestStat 4.10 0.251 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value Ctrl 100.00

CCLI	100.00	•	•
Dose1	100.00	1.000	0.020
Dose2	100.00	1.000	0.076
Dose3	100.00	1.000	0.150
CIRCAN DIZ			
SUMMARY		NOAEC	LOAEC
MannWh	, , ,	Dose3	>highest dose
Jonckh	eere	Dose3	>highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE NH (Number Hatched)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion

Shapiro-W Test St	at I	piro-Wilks -value	Levenes Test Sta	at P-value	Conclusion	
0.981		0.452	2.240	0.093	USE PARAMETRIC	TESTS
*****	*****	*****	*****	*****	*****	*****
BASIC SUMMA	RY STATIS	STICS				
Level N	Mean	StdDev	StdErr	Coef of V	ar 95% Conf.I	interval
Ctrl 15	34.60	18.75	4.84	54.18	24.22,	44.98
Dosel 16	28.56	17.87	. 4.47	62.58	19.04,	38.09
Dose2 15	28.13	12.79	3.30	45.46	21.05,	35.22
Dose3 16	18.50	11.71	2.93	63.28	12.26,	24.74
Level	Median	Min	Max	%of Control(means) %Reduct	ion(means)
Ctrl	41.00	0.00	63.00	•		
Dose1	29.00	0.00	58.00	82.55	17.4	15
Dose2	26.00	0.00	47.00	81.31	18.6	59
Dose3	21.00	0.00	44.00	53.47	46.5	3

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df Denominator df F-stat P-value 3 58 2.85 0.045

Dunnett - testing each trt mean signif. less than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOAEC or LOAEC

Level	Mean	Dunnett	Isotonic	Williams	4		Tukey p-v	alues	
		p-value	mean	p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl	34.60	•	34.60	-	0.704	0.668	0.028		•
Dose1	28.56	0.292	28.56	0.170		1.000	0.271		•
Dose2	28.13	0.270	28.13	0.165	•	•	0.322		•
Dose3	18.50	0,008	18.50	0.003	•	•	•	•:	•
SUMMAR	Y		NOAEC		LOAEC				•
Dunn	ett		Dose	2	Dose3				
Will:	iams		Dose	2	Dose3				

PMRA Submission Number

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE NH EL (NumberHatched/EggsLaid (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.830 <.001 1.833 0.151 USE NON-PARAMETRIC TESTS ************************* BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval 3.92 14.66 65.39, Ctrl 14 73.86 19.85 57.94 26.24 62.58 22.38 54.35 24.70 6.56 45.28 43.96, Dosel 16 71.92 Dose2 15 5.78 35.77 50.18, 74.97 6.18 Dose3 16 24.70 54.35 45.44 67.51 41.19, Max Level Median Min %of Control (means) %Reduction (means) Ctrl 76.39 25.00 86.00 0.00 78.45 21.55 Dose1 68.26 80.56 Dose2 63.49 0.00 85.19 84.72 15.28 0.00 Dose3 60.14 89.66 73.59 26.41 ************************* NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 10.51 0.015 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend

Level Ctrl	Median 76.39	MannW	Mit(Bon	adjust)	p-value	Jonckheere p-va	alue
Dose1	68.26			0.034		0.007	
Dose2	63.49			0.215	the state of	0.041	
Dose3	60.14	* * * * * * * * * * * * * * * * * * * *		0.004		0.003	
SUMMARY			NOAEC		LOAEC		-
MannWhit	(Bonf	adjust)		st dose	Dose1		

<lowest dose</pre>

PMRA Submission Number

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE NH ES (NumberHatched/EggsSet (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha+level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.817 <.001 2.019 0.121 USE NON-PARAMETRIC TESTS ************************* BASIC SUMMARY STATISTICS Level N StdDev StdErr Coef of Var 95% Conf.Interval Mean 14.54 Ctrl 14 Dosel 16 3.89 85.35 76.95, 17.04 30.08 49.84, 81.90 65.87 7.52 45.66 Dose2 15 71.10 24.67 6.37 34.70 57.44, 84.76 Dose3 16 63.51 7.05 78.53 28.19 44.39 48.49, Level Median % of Control (means) % Reduction (means) Min Max Ctrl 87.30 38.46 100.00 77.18 Dose1 75.89 0.00 91.30 22.82 Dose2 71.43 0.00 83.30 95.83 16.70 71.96 0.00 96.30 74.41 25.59 ************************************ NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 10.18 0.017 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value Ctrl 87.30 Dose1 75.89 0.028 0.006 Dose2 71.43 0.144 0.030 Dose3 71.96 0.006 0.004 SUMMARY NOAEC LOAEC MannWhit (Bonf adjust) <lowest dose Dose1

<lowest dose</pre>

PMRA Submission Number

MannWhit (Bonf adjust)

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE NH LE (NumberHatched/LiveEmbryo (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value <.001 0.105 0.870 2.154 USE NON-PARAMETRIC TESTS *********************** BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval Ctrl 14 94.86 4.38 1.17 4.62 92.33, 86.13 10.24 89.30 7.54 80.16 14.96 80.22, Dosel 14 2.74 11.89 92.05 2.01 Dose2 14 8.44 84.94, 93.65 Dose3 14 4.00 18.66 71.52, 88.80 Max %of Control(means) Level Median Min %Reduction(means) 87.23 Ctrl 94.89 100.00 9.20 Dose1 90.48 58.82 95.45 90.80 Dose2 87.82 76.92 100.00 94.13 5.87 36.84 82.91 100.00 84.50 15.50 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 15.46 0.001 MannWhit (Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value Ctrl 94.89 90.48 0.017 Dose1 0.003 Dose2 87.82 0.082 0.017 0.002 Dose3 82.91 <.001 SUMMARY NOAEC LOAEC

<lowest dose

<lowest dose

Dose1

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE HS (Hatching Survival(d14))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS
Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value

0.982 0.518 2.298 0.087 USE PARAMETRIC TESTS

********	******	*****	******	*****	*****	****
BASIC SUMMAR	RY STATIST	CICS				
Level N	Mean	StdDev	StdErr	Coef of Var	95% Conf.In	terval
Ctrl 15	34.07	18.32	4.73	53.78	23.92,	44.21
Dosel 16	28.38	17.73	4.43	62.50	18.92,	37.83
Dose2 15	27.60	12.65	3.27	45.83	20.60,	34.60
Dose3 16	16.56	11.37	2.84	68.66	10.50,	22.62
Level	Median	Min	Max	%of Control(means)	%Reducti	on(means)
Ctrl	41.00	0.00	63.00	•	•	
Dose1	29.00	0.00	58.00	83.29	16.71	* **
Dose2	25.00	0.00	46.00	81.02	18.98	
Dose3	16.00	0.00	44.00	48.62	51.38	
					,	·

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests

Analysis of Variance (ANOVA) - overall F-test

Numerator df Denominator df F-stat P-value 3 58 3.57 0.019

Dunnett - testing each trt mean signif. less than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOAEC or LOAEC

Level	Mean	Dunnett p-value	Isotonic mean	Williams p-value	Dose1	Dose2	Tukey p-v	values Dose4	Dose5
Ctrl Dosel Dose2 Dose3	34.07 28.38 27.60 16.56	0.309 0.264 0.003	34.07 28.38 27.60 16.56	0.182 0.160 0.001	0.730	0.656 0.999	0.012 0.140 0.198	•	:
SUMMARY Dunne Willi	tt		NOAEC Dose2 Dose2		LOAEC Dose3 Dose3				

PMRA Submission Number

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE HS ES (HatchingSurvival/EggsSet (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.854 <.001 2.099 0.110 USE NON-PARAMETRIC TESTS ************************ BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval Ctrl 14 84.31 14.47 3.87 17.16 75.96, 29.95 7.49 49.55, Dosel 16 65.51 45.72 81.47 Dose2 15 Dose3 16 69.73 24.27 6.27 34.81 56.29, 83.17 55.75 26.97 6.74 70.12 48.37 41.38, Max Level Median Min %of Control(means) %Reduction(means) 86.46 38.46 Ctrl 100.00 77.70 Dose1 74.54 0.00 22.30 91.30 Dose2 71.43 0.00 94.12 82.70 17.30 Dose3 59.58 0.00 88.89 66.12 33.88 ************************ NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 14.20 0.003 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value Ctrl 86.46 Dose1 74.54 0.031 0.007 Dose2 71.43 0.121 0.023 Dose3 59.58 0.002 < .001 SUMMARY NOAEC LOAEC MannWhit (Bonf adjust) <lowest dose</pre> Dosel

<lowest dose</pre>

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE HS NH (HatchingSurvival/NumberHatched (%)) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.642 <.001 11.144 <.001 USE NON-PARAMETRIC TESTS ******************** BASIC SUMMARY STATISTICS Mean StdDev StdErr Coef of Var 95% Conf.Interval Level N 98.82 99.47 Ctrl 14 2.22 0.59 2.25 97.54, 100.00 1.07 98.85, 1.08 Dosel 14 0.29 100.00 Dose2 14 98.07 2.52 0.67 2.57 96.62, 99.53 Dose3 14 88.02 15.94 4.26 78.81, 97.22 18.11 Level Median Min Max %of Control (means) %Reduction (means) Ctrl 100.00 92.59 100.00 Dose1 100.00 97.14 100.00 100.66 -0.66 0.76 Dose2 100.00 92.31 99.24 100.00 Dose3 92.58 44.44 100.00 89.07 10.93 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 15.77 0.001 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend

Level Ctrl Dose1 Dose2 Dose3	Median 100.00 100.00 100.00 92.58	MannW	hit(Bon	adjust)p 1.000 1.000 0.012	o-value	0.	737 145 001	⁄alue
SUMMARY MannWh Jonckh	•—	adjust)	NOAEC Dose2 Dose2		LOAEC Dose3 Dose3			

PMRA Submission Number

MannWhit (Bonf adjust)

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE THICK (Eggshell thickness) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat Test Stat P-value P-value 0.599 <.001 1.510 0.221 USE NON-PARAMETRIC TESTS ********************************* BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval 0.10 Ctrl 15 Dosel 16 0.35 0.03 0.30, 28.64 0.41 0.38 0.37 0.02 0.01 8.21 0.36, 0.40 Dose2 15 0.36, 0.01 5.42 0.38 0.03 Dose3 16 0.35 0.01 0.37 9.08 0.33, Level Median Min Max %of Control (means) %Reduction(means) 0.45 Ctrl 0.37 0.00 107.12 0.37 -7.12Dose1 0.34 0.45 Dose2 0.37 0.33 0.40 105.10 -5.10 Dose3 0.36 0.26 98.46 0.39 1.54 ******************** NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 7.87 0.049 MannWhit (Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median MannWhit(Bon adjust)p-value Jonckheere p-value Ctrl 0.37 Dose1. 0.37 1.000 0.578 Dose2 0.37 1.000 0.512 Dose3 0.36 0.067 0.015 SUMMARY NOAEC LOAEC

Dose3

Dose2

>highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902
ANALYSIS RESULTS FOR VARIABLE HATWT (Hatchling Weight)

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS
Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01

Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05
Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

Shapiro-Wilks	Shapiro-Wilks	Levenes	Levenes	Conclusion	, ,
Test Stat	P-value	Test Stat	P-value		*
0.554	<.001	0.674	0.572	USE NON-PARAMET	RIC TESTS

******	*****	*****	*****	*****	·****	*****
BASIC SUM	MARY STATIST	rics				
Level N	Mean	StdDev	StdErr	Coef of Var	95% Conf.In	terval
Ctrl 1	5 30.40	8.61	2.22	28.32	25.63,	35.17
Dosel 1	6 29.19	11.62	2.90	39.80	23.00,	35.38
Dose2 1	5 31.40	8.90	2.30	28.35	26.47,	36.33
Dose3 1	6 28.81	11.45	2.86	39.74	22.71,	34.91
Level	Median	Min	Max %	of Control(means)	%Reducti	on(means)
Ctrl	32.00	0.00	36.00	•	•	
Dose1	33.00	0.00	38.00	96.01	3.99	
Dose2	34.00	0.00	37.00	103.29	-3.29	
Dose3	32 50	0.00	37 00	94 78	5 22	

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Kruskal-Wallis test - equality among treatment groups
Degrees of Freedom TestStat P-value

3 1.94 0.585

MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon	adjust)p-value	Jonckheere p-value
Ctrl	32.00		. •	•
Dose1	33.00		1.000	0.602
Dose2	34.00		1.000	0.895
Dose3	32.50		1.000	0.678
		-		

SUMMARY NOAEC LOAEC

MannWhit (Bonf adjust) Dose3 >highest dose
Jonckheere Dose3 >highest dose

PMRA Submission Number

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE SURVWT (Survivor Wt (d14))

TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS

Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses.

DASIC SU	IMMATE	CI STATIS	TICS		and the second s		
Level	N	Mean	StdDev	StdErr	Coef of Var	95% Conf.Interval	
Ctrl	15	277.07	79.72	20.58	28.77	232.92, 321.21	
Dose1	16	256.31	102.64	25.66	40.04	201.62, 311.00	
Dose2	15	259.13	78.46	20.26	30.28	215.68, 302.59	
Dose3	16	234.19	95.23	23.81	40.67	183.44, 284.93	
Level		Median	Min	Max	%of Control(means) %Reduction(means)	
Ctrl		300.00	0.00	346.00	•	•	
Dose1		289.00	0.00	332.00	92.51	7.49	
Dose2		281.00	0.00	329.00	93.53	6.47	
Dose3		272.00	0.00	302.00	84.52	15.48	
						•	

NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 7.47 0.058

MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend

Level	Median	MannWhit(Bon	adjust) p	o-value	Jonckheere p-value	
Ctrl	300.00		•		•	
Dose1	289.00		1.000		0.391	
Dose2	281.00	*	0.358		0.125	
Dose3	272.00		0.029		0.004	
SUMMARY		NOAEC		LOAEC		
MannWhi	it (Bonf adju:	st) Dose2		Dose3		
Jonckhe	eere	Dose2		Dose3		

PMRA Submission Number

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE FOOD (Food Consumption) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Conclusion Levenes Levenes Test Stat P-value Test Stat P-value 0.938 0.004 1.043 0.381 USE NON-PARAMETRIC TESTS BASIC SUMMARY STATISTICS Coef of Var 95% Conf.Interval Level N Mean StdDev StdErr Ctrl 15 Dosel 16 135.73 27.53 7.11 120.49, 150.98 20.28 133.27, 145.06 22.14 5.53 15.26 156.86 16.89 Dose2 15 136.40 4.36 12.39 127.04, 145.76 Dose3 16 133.63 19.88 4.97 14.88 123.03, 144.22 Level Median %of Control (means) Min Max %Reduction (means) Ctrl 133.00 100.00 199.00 Dose1 139.50 111.00 195.00 106.87 -6.87 Dose2 133.00 115.00 100.49 -0.49 180.00 128.50 102.00 171.00 98.45 1.55 ************************************** NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3.26 0.353 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend Level Median Jonckheere p-value MannWhit(Bon adjust)p-value Ctrl 133.00 Dose1 139.50 1.000 0.890 Dose2 133.00 1.000 0.607 128.50 Dose3 1.000 0.281 SUMMARY NOAEC LOAEC MannWhit (Bonf adjust) Dose3 >highest dose

Dose3

>highest dose

PMRA Submission Number

Dose3

Mallard repro, Metaldehyde, MRID 42867902

3.00 -249.00

EPA MRID Number 42867902

-156.12

ANALYSIS RESULTS FOR VARIABLE WTGAINM (Male wt gain) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance (absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Levenes Conclusion Test Stat P-value Test Stat P-value 0.977 0.311 1.740 0.169 USE PARAMETRIC TESTS **************************** BASIC SUMMARY STATISTICS Level N Mean StdDev StdErr Coef of Var 95% Conf.Interval -6.47 Ctrl 15 73.48 18.97 -1136.28 -47.16,Dosel 16 -36.50 111.00 27.75 -304.11 -95.65, 22.65 Dose2 15 7.60 76.04 19.63 1000.58 -34.51,49.71 Dose3 16 106.70 -73.42, -644.23 -16.5626.68 40.29 Level Median Min Max %of Control (means) %Reduction (means) 10.00 Ctrl -152.00 114.00 -18.00 -218.00 564.43 -464.43Dose1 195.00 -117.53 Dose2 12.00 -191.00 88.00 217.53

256.12

116.00

PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests
Analysis of Variance (ANOVA) - overall F-test

Numerator df Denominator df F-stat P-value
3 58 0.61 0.614

Dunnett - testing each trt mean signif. less than control
Williams - test assumes dose-response relationship, testing negative trend
Tukey - two-sided tests, all possible comparisons, not used for NOAEC or LOAEC

		Dunnett	Isotonic	Williams			Tukey p-	values	
		p-value	mean	p-value	Dose1	Dose2	Dose3	Dose4	Dose5
Ctrl -	6.47	•	-6.47	·	0.810	0.977	0.991		
Dose1 -3	6.50	0.368	-15.16	0.472	•	0.563	0.932		
Dose2	7.60	0.871	-15.16	0.504	. •	•	0.891	•.	•
Dose3 -1	6.56	0.628	-16.56	0.500	•	. •	•		•
SUMMARY Dunnett William:			NOAEC Dose Dose	3		st dose st dose			

PMRA Submission Number

MannWhit (Bonf adjust)

Jonckheere

EPA MRID Number 42867902

Mallard repro, Metaldehyde, MRID 42867902 ANALYSIS RESULTS FOR VARIABLE WTGAINF (Female wt gain) TESTS OF ASSUMPTIONS FOR PARAMETRIC ANALYSIS Shapiro-Wilks test for Normality of Residuals -- alpha-level=0.01 Levenes test for homogeneity of variance(absolute residuals) -- alpha-level=0.05 Use parametric analyses if neither test rejected, otherwise non-parametric analyses. Shapiro-Wilks Shapiro-Wilks Levenes Conclusion Levenes Test Stat P-value Test Stat P-value 0.721 <.001 1.036 0.383 USE NON-PARAMETRIC TESTS *********************** BASIC SUMMARY STATISTICS Level N StdDev StdErr Coef of Var 95% Conf.Interval Mean 249.02 104.73 Ctrl 15 260.81 67.34 -39.70, 249.16Dosel 16 -33.03, 14.50 89.20 22.30 615.17 62.03 Dose2 15 59.40 86.69 22.38 145.94 11.39, 107.41 Dose3 16 36.75 127.46 31.86 346.82 -31.17, 104.67Level Median %of Control(means) %Reduction (means) Min Max Ctrl 71.00 -93.00 1007.00 86.16 13.84 Dosel 12.00 -182.00 224.00 Dose2 42.00 -84.00 198.00 56.72 43.28 16.00 -155.00 35.09 301.00 NON-PARAMETRIC ANALYSES - use alpha-level=0.05 for all tests Kruskal-Wallis test - equality among treatment groups Degrees of Freedom TestStat P-value 3 1.90 0.593 MannWhit(Bon) - testing each trt median signif. less than control Jonckheere - test assumes dose-response relationship, testing negative trend MannWhit(Bon adjust)p-value Level Median Jonckheere p-value . Ctrl 71.00 0.103 Dose1 12.00 0.334 1.000 0.508 Dose2 42.00 1.000 Dose3 16.00 0.428 SUMMARY NOAEC LOAEC

Dose3

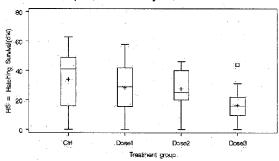
Dose3

>highest dose

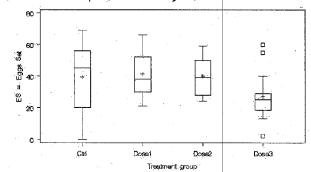
>highest dose

Box Plots:

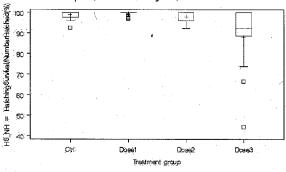
Mallard repro, Metaldehyde, MRID 42867902



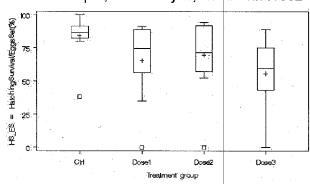
Mallard repro, Metaldehyde, MRID 42867902



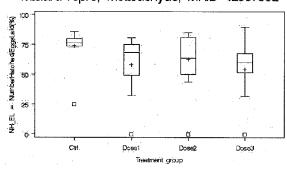
Mallard repro, Metaldehyde, MRID 42867902



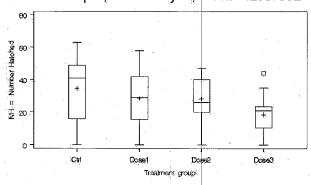
Mallard repro, Metaldehyde, MRID 42867902



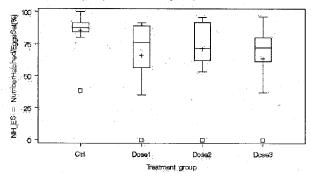
Mallard repro, Metaldehyde, MRID 42867902



Mallard repro, Metaldehyde, MRID 42867902



Mallard repro, Metaldehyde, MRID 42867902



Mallard repro, Metaldehyde, MRID 42867902

